Academic Detailing to Improve Use of Broad-Spectrum Antibiotics at an Academic Medical Center

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Background: Antibiotic misuse is common and costly and may promote antibiotic resistance. We tested the efficacy of a targeted one-on-one educational program ("academic detailing") designed to improve the appropriateness of broad-spectrum antibiotic use.

Methods: A randomized controlled trial was conducted in a large US teaching hospital. During an 18-week study period, 17 general medical, oncology, and cardiology services either received academic detailing or did not. The intervention was prompted by an order for either levofloxacin or ceftazidime that led to a computer-based review of data for that patient. Orders for the 2 target antibiotics deemed unnecessary by a priori criteria were included in the study. The primary outcome examined was the number of days that unnecessary levofloxacin or ceftazidime was administered in intervention and control groups.

Results: Before the trial, intervention and control services had similar prescribing patterns for the target antibiotics; the drugs were used for similar indications throughout the study period. During the intervention, there was a reduction of 37% in days of unnecessary levofloxacin or ceftazidime use per 2-week interval on services randomized to the educational intervention vs control services ($P<.001$). In multivariable analyses controlling for baseline prescribing and study interval, the rate of unnecessary use of the 2 target antibiotics was reduced by 41% on the intervention services compared with controls (95% confidence interval, 44%-78%; $P<.001$). Length of stay, intensive care unit transfers, readmission rates, and in-hospital death rates were similar in both groups ($P\geq.10$ for all).

Conclusion: Targeted one-on-one education is a practical, effective, and safe method for reducing excessive broad-spectrum antibiotic use.

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ANTIBIOTIC MISUSE is common and costly. Approximately one third of all hospitalized patients receive an antibiotic, and several reports[1-3] suggest that at least half of antibiotic orders are unnecessary, poorly chosen, or incorrectly dosed. Physicians often opt for broad-spectrum antibiotics when a narrower-spectrum agent would suffice. A review of 2 months of vancomycin hydrochloride use at one teaching hospital found that 70% of orders were inappropriate; problematic orders were as common for the medical service as they were for the surgery service.[1]

Suboptimal use of antibiotics poses problems beyond those applicable to the individual patient so treated; overreliance on broad-spectrum agents is also thought to be an important contributor to growing worldwide antimicrobial resistance.[4] A recent study[5] found that as quinolone use increased more than 6-fold between 1988 and 1997, from 0.8 to 5.5 per 100 persons per year, the prevalence of pneumococci with reduced susceptibility to quinolones increased from 0% to 1.7%. Quinolone-resistant *Salmonella enterica* and *Campylobacter jejuni* infections have also been increasingly reported.[6,7] New antimicrobial resistance has emerged in many different human pathogens, and rates of existing resistance have increased. At least 6 studies[8-13] have suggested that rates of invasive infections with drug-resistant *Streptococcus pneumoniae* are related to recent antibiotic exposure, and 1 recent study[14] suggested that local antibiotic use patterns directly affected local resistance patterns. These data have prompted a working group of the Centers for Disease Control and Prevention to focus attention on the judicious use of antibiotics as one part of the strategy to combat drug-resistant *Streptococcus pneumo-*

PARTICIPANTS AND METHODS

STUDY SITE

Brigham and Women's Hospital is a 697-bed academic medical center affiliated with Harvard Medical School in Boston, Mass. Approximately 32% of admissions are to the internal medicine department, including general medical, oncology, and cardiology services. A typical service consists of 1 attending physician, 1 second- or third-year medical resident, and 2 interns; interns and residents write all antibiotic orders.

To achieve balanced patient groups for the present study, we assigned services to intervention or control status using a blocked randomization design. Three of the general medical services were randomly assigned to intervention and 3 to control, and 2 of the oncology services were randomly assigned to intervention and 2 to control. Three additional general medical services and 4 cardiology services were added at week 5 through a similar blocked random assignment approach. In all, 9 services comprised the intervention group and 8 the control group. The study period began January 20, 1999, and ended May 19, 1999; the 4 weeks immediately preceding this period were considered the baseline period.

TARGET ORDERS

We used the hospital's computerized pharmacy records to review all orders for levofloxacin and ceftazidime written for patients on the intervention and control teams. The hospital's Division of Infectious Diseases developed a set of guidelines for first-line antibiotic therapy, including recommendations for the proper use of these agents. We disseminated these guidelines to all house officers as pocket-sized laminated brochures (available on request) before this study. Although in any given situation many antibiotics may be effective, these guidelines recommended preferred antibiotic choices for our hospital.

Each morning, a research assistant reviewed computerized laboratory, pharmacy, and prior admission data for all patients for whom physicians ordered levofloxacin or ceftazidime in the prior 24 hours. The criteria were applied without regard to the study group assignment. All orders for levofloxacin were flagged for review unless the patient had (1) an isolate sensitive to levofloxacin, (2) a history

of a solid organ transplantation or long-term use of immunosuppressive medications, (3) multiple antibiotic allergies, or (4) serum creatinine levels of more than 1.5 mg/dL (132.6 μmol/L). For ceftazidime, orders were also flagged unless the patient had (1) an isolate sensitive to ceftazidime; (2) an absolute neutrophil count of less than 500/mm^3; (3) a history of a solid organ transplantation, cystic fibrosis, or long-term use of immunosuppressive medications; (4) multiple antibiotic allergies; or (5) resided in an institutional setting within 1 week of hospital admission. Henceforth, we will use the term *unnecessary use* for the orders that fell outside the guidelines and were flagged for review. We excluded orders for patients in whom any of the following occurred on the date their target order was reviewed: death, discharge, transfer to an intensive care unit, or surgery. The remaining orders formed the study cohort. On the intervention services, levofloxacin or ceftazidime orders judged to be unnecessary prompted one of the academic detailers to review the patient's full medical record and contact the responsible intern or resident. No contact occurred for orders written for patients on teams randomized to the control condition.

INTERVENTION

The educational intervention was directed at interns and residents on the intervention teams who wrote unnecessary orders for either of the 2 broad-spectrum antibiotics studied. The educational intervention, which used an academic detailing approach, was conducted by 3 clinician-educators, 2 infectious diseases physicians, and 1 specially trained clinical pharmacist.[18,19] The educators were trained through participating in practice sessions, with several of the authors (D.H.S. and J.A.) using scripts and role-playing exercises.

The intern who wrote the original order was the primary contact, but resident physicians were contacted if the intern was unavailable. Academic detailers presented information to the intern or resident physicians interactively in a case-relevant, concise manner, stressing microbiologic data, local resistance patterns, and the clinical literature. The interns and residents were not aware that their ordering patterns were being studied. The detailers provided each ordering physician with a copy of the guidelines and made suggestions for alternative regimens based

niae.[15] Although antimicrobial resistance is complex and multifactorial, there is evidence that reducing the use of broad-spectrum antibiotics may result in improved microbial susceptibility.[16]

In most hospitals, antibiotics account for more than 10% of pharmacy expenditures, and the additional cost of antibiotic resistance is substantial. A report from the US Office of Technology Assessment estimated that the extra hospital costs associated with drug-resistant nosocomial bacterial infections were $1.3 billion annually.[17] In our institution, drug use evaluations have suggested that narrower-spectrum antibiotics could be safely substituted for a substantial number of broad-spectrum antibiotic orders. However, most patients are never seen by infectious disease consultants; thus, there is no routine method for such antibiotic optimization. Given increas-

ing concern over unnecessary patient exposure to broad-spectrum antibiotics, trends in antimicrobial resistance patterns, and the costs associated with both, we undertook the present study to determine whether one-on-one education by clinical specialists on a patient-specific basis ("academic detailing") could reduce excessive use of broad-spectrum antibiotics.

RESULTS

More than 4500 patients were admitted to the intervention and control services during the baseline and study periods. Patient characteristics on both sets of services were similar and did not differ between the baseline and study periods (**Table 1**). At baseline, the mean±SD number of days of unnecessary target antibiotic use was

on these recommendations, but the final drug choice was always left to the interns and residents. The clinician-educators also distributed graphs and summaries of resistance patterns in our institution and trends in the utilization and cost of antibiotics (available on request). The encounter took place over the telephone if neither intern nor resident was available to meet in person; this occurred in 32 episodes. In 4 instances, the responsible intern or resident was unavailable to meet or speak by telephone; e-mail messages were sent to the interns in these cases. All encounters were included in the intervention group. Face-to-face or telephone sessions generally lasted 10 minutes. In 14 instances, the academic detailer decided not to contact either intern or resident after reviewing the chart. This was primarily because prior infectious disease consultants had recommended one of the targeted antibiotics. These orders were included in all analyses.

DATA COLLECTION

The main study end point was the average number of days that unnecessary levofloxacin or ceftazidime was administered per service. This outcome was compared for each 2-week interval for services in the intervention vs control groups. The prescribing information was drawn from the hospital's computerized pharmacy records. In a subsample of patients, we validated the computerized pharmacy data against the manually completed medication administration records in the patient's hospital chart. There was complete agreement in 14 (93%) of 15 patient records examined and partial agreement in the 1 remaining record. Patients who were prescribed more than one new course of levofloxacin or ceftazidime were counted in the analysis more than once. We also reviewed the medical records of all patients in both the intervention and control groups to determine the presumed source of infection that prompted the target antibiotic order. Next, medication orders for the day of the educational intervention (or the comparable day on the control services) were examined to determine whether the target drug regimens were continued, discontinued, or changed in route or dosage. Finally, we examined computerized records for every patient admitted to intervention or control services during the study period to measure rates of death and transfer to an intensive care unit, length of stay, and readmission within 30 days of discharge.

ANALYSIS

We compared the average number of days of unnecessary levofloxacin and ceftazidime use during each 2-week interval for the intervention and control services. To calculate the expected values and confidence intervals (CIs) and to test differences, we used a linear univariate fixed-effects model (PROC MIXED).[20] Since we suspected that differences in baseline prescribing and duration of the intervention would be important confounders, multivariable models were constructed including these factors as independent variables. The dependent variable was unnecessary prescribing of the target antibiotics during each 2-week interval of the intervention period. To estimate the relative reduction in unnecessary use of target antibiotics in the intervention group, we used a fixed-effects model (PROC GENMOD in SAS statistical software).[20] This model used a log-linear link function, assumed a Poisson distribution, and accounted for overdispersion. Experimental group assignment (intervention or control) was the independent variable of interest, the individual service was considered a class effect, and covariates included level of baseline prescribing and time, modeled as both a linear and categorical effect. The interaction between assignment and time was also assessed. We further considered a linear random-effects model to account for variation between services (PROC MIXED in SAS statistical software)[20]; the results of this analysis were similar to those found in the fixed-effects models with respect to the level of statistical significance, and only the fixed-effects model results are presented.

All analyses were conducted on an intention-to-treat basis. Several services had unusually heavy prescribing of the target antibiotics during certain 2-week blocks. To examine the effect of such periods, we performed identical analyses of the main effect after removing these outlier intervals from the analyses. The results were nearly identical; thus, only the analyses using all data points will be presented. Finally, we assessed the mean length of stay for all patients on intervention and control services and measured the proportion of patients who were transferred to an intensive care unit, were readmitted to Brigham and Women's Hospital within 30 days of discharge, or died in the hospital. We examined these secondary outcomes not only for patients who received the target antibiotics, but also for every patient admitted to a study service during the baseline and intervention periods.

8.5±7.8 per 2-week interval for the intervention service and 7.6±4.7 for the control services (*P*=.80) (**Figure 1**).

During the 18-week study period, 490 patients from all study services were prescribed levofloxacin or ceftazidime, the target antibiotics. Computerized record review indicated that 212 patients were not appropriate for study for the following reasons: 83 were discharged, transferred to an intensive care unit, taken to surgery on the index date, or died; 37 had serum creatinine levels greater than 1.5 mg/dL (>132.6 µmol/L); 23 had a known isolate sensitive to one of the target antibiotics; 21 had a history of a solid organ transplantation or were taking immunosuppressive medications; 20 who were prescribed ceftazidime had an absolute neutrophil count less than 500/mm³; 18 had multiple antibiotic allergies; and 10 who were prescribed ceftazidime had cystic fibrosis and were

at high risk of pseudomonal infections. The remaining 278 unnecessary prescriptions in 260 patients formed the study cohort. Among these patients, the indications for treatment or presumed sources of infection were similar for those in the intervention and control groups (**Table 2**). There were slightly higher rates of fever and neutropenia among levofloxacin users on the intervention services (*P*=.04).

We then examined the mean number of days of unnecessary target antibiotic use per 2-week interval per service for each group (Figure 1). Although baseline prescribing was similar, during the intervention period, the number of days of unnecessary use of target antibiotics was 37% lower for the intervention services than for controls (*P*<.001) (Figure 1). During the study period, there were a mean±SD of 5.5±2.1 days per 2-week interval for

Table 1. Characteristics of Study Services*

Characteristics	Intervention Services (n = 9)	Control Services (n = 8)
Baseline period		
Admissions per 2 wk per service, mean ± SD	26 ± 4	25 ± 4
Age, mean ± SD, y	61 ± 4	60 ± 5
Sex, % female	52	48
Study period		
Admissions per 2 wk per service, mean ± SD	27 ± 4	25 ± 2
Age, mean ± SD, y	60 ± 5	60 ± 4
Sex, % female	51	53

*$P>.30$ for all.
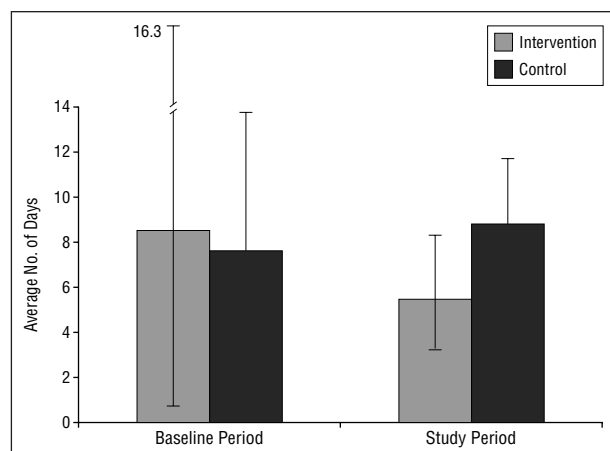
Figure 1. Average number of days of unnecessary use of target antibiotics per 2-week interval per service. $P<.001$ for the difference between intervention and control groups during the study period. For the study period, confidence intervals were calculated from the univariate fixed-effects model. See text for description of "unnecessary use of target antibiotics."

Table 2. Presumed Source of Infection During Study Period*

Infection Source	Intervention Services, %	Control Services, %	P
Genitourinary	23	20	.52
Respiratory	46	43	.53
Intra-abdominal	14	19	.32
Joint, bone, skin, soft tissue	9	9	.94
Sepsis, line or not otherwise specified	5	5	.91
Fever and neutropenia	5	1	.04
Central nervous system	0	1	.23

*A total of 260 patients accounted for the 278 orders included in the study. There were 125 study orders in the intervention services group and 153 in the control services group. Columns do not add to 100% because of rounding. Genitourinary includes urosepsis and urinary tract infections. Respiratory includes upper and lower tract infections.
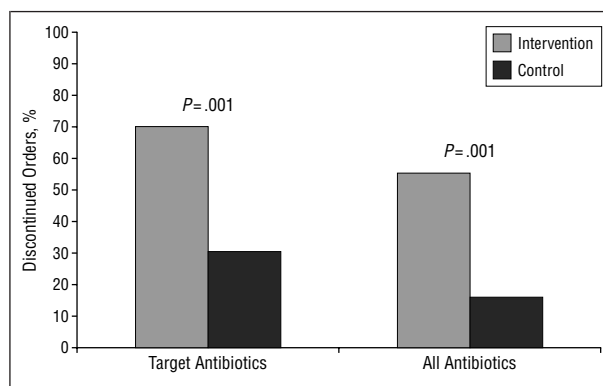
Figure 2. Antibiotic prescribing during intervention. The day the target order was identified and the next calendar day were examined to determine these patterns. P values are from χ^2 tests and refer to the difference between intervention and control groups.

the intervention services vs 8.8±2.2 days for the controls; this reduction was because of 28 fewer starts and an average antibiotic course 0.8 day shorter. The multivariate analyses, accounting for repeated measures of the target antibiotics and baseline prescribing, indicated that the risk of receiving a day of unnecessary target antibiotic was reduced by 41% on the intervention services compared with controls (95% CI, 44%-78%; $P<.001$). There did appear to be an effect of time on the intervention, such that the risk of prescribing an unnecessary day of the target antibiotics continued to decline throughout the entire study period. However, no interaction was found between group assignment and time ($P=.48$). During the study period, prescribing of the target antibiotics throughout the hospital on nonstudy services remained stable: 1874 days of target antibiotics administered per 2-week interval during the baseline period vs 1882 days during the intervention period ($P=.40$).

We next examined prescribing of unnecessary target antibiotics on the day that the order was identified and the subsequent day (**Figure 2**). For the intervention services, 88 (70%) of these orders were discontinued, whereas only 46 orders (30%) for the control services were discontinued ($P=.001$). For the intervention services, 69 patient orders (55%) for unnecessary target antibiotics had all antibiotic use discontinued. This significantly differed from the control services in which only 24 patient orders (16%) were followed by discontinuation of all antibiotic use ($P=.001$). Route changes (intravenous to oral) were equal and uncommon (14%) for both intervention and control services.

The intervention had no measurable negative clinical effects. The average length of stay, proportion of patients transferred to an intensive care unit or patients readmitted within 30 days of discharge, and death rates were similar for all patients in the intervention and control services (**Table 3**).

COMMENT

Reduction of inappropriate use of antibiotics, especially broad-spectrum agents, is an important goal in acute care settings such as teaching hospitals. In a randomized controlled trial that took place in the department of medicine of a US academic medical center, we found that the risk of prescribing a day of unnecessary target antibiotic was 41% lower on services randomized to a intervention of "academic detailing" compared with controls. This significant effect of the intervention remained after adjusting for baseline prescribing, clustering of repeated mea-

sures within a given service, and duration of the intervention. Both fewer starts and shorter courses of target antibiotics account for the reduction of use of broad-spectrum antibiotics in the intervention services. This suggests that to some degree interns and residents learned not to prescribe an unnecessary antibiotic but that the daily academic detailing reminded prescribing physicians to stop the use of previously started but unnecessary antibiotics.

The intervention was based on the academic detailing approach developed by our group that has proven to be a useful method for improving behavior in a variety of prescribing situations.[18-22] Academic detailing is a program of one-on-one interactive educational outreach provided by a clinician, either a pharmacist or physician, who has been trained to discuss prescribing decisions with physicians in a manner likely to induce evidence-based practice change. An academic detailing approach has been used successfully to improve outpatient antibiotic use, but not inpatient prescribing, to our knowledge.[18,23,24]

Several limitations of the present study should be considered. Since resident physicians switched services every month, contamination occurred between intervention and control groups. This would have biased the results against finding any difference between intervention and control teams and thus may have dampened the observed effect of the intervention. One method for dealing with this potential would have been to randomize physicians; however, many of the decisions regarding antibiotic orders are made by the team and thus randomization by a physician would have allowed for substantial intrateam contamination. Fourteen orders were included in the intervention set that were not deemed appropriate for academic detailing because the antibiotics had been suggested by a prior consultation from the infectious diseases division. We kept these orders in the analysis since they were part of the original randomization set; their inclusion reduced the effect of the intervention. Finally, although we did not collect specific data from house officers about why they continued using possibly unnecessary antibiotics, possible reasons include misinformation, neglect of microbiologic laboratory information, pressure from attending physicians, and patient or family concerns.[25]

Part of the success or failure of the academic detailing intervention rests on the ability and availability of the educators doing the one-on-one intervention. We attempted to minimize the effect of the detailer's personal style on the study outcome by standardizing the educational encounter through the use of scripts and a common evidence-based approach. In addition, many hospitals may not have infectious disease consultants available to perform the academic detailing. Our intervention used a trained clinical pharmacist whose impact on prescribing was similar to that of the infectious disease physicians; previous interventions have likewise used pharmacist-educators with good effects.[18,21]

Other than the one-time initial costs of developing and printing antibiotic guidelines for our hospital, the daily costs of conducting the intervention included approximately 1 hour of a research assistant's time to re-

Table 3. Secondary Outcomes

Outcome	Intervention Service Patients (n = 2624)	Control Service Patients (n = 2489)	P*
Average length of index admission, mean ± SD, d	4.8 ± 6.0	4.8 ± 5.5	.94
Rehospitalization within 30 d, %	4.0	3.3	.13
Intensive care unit transfer, %	6.6	6.4	.71
Death during index admission, %	2.3	2.2	.90

*P values are from χ^2 test for dichotomous outcomes and t test for continuous ones.

view new orders for the target antibiotics and 1 hour from an academic detailer; thus, the estimated annual cost was $21 750. Although a formal economic analysis was not performed, we found that the length of antibiotic courses was shortened on the services randomized to the intervention: 55% of patients had all antibiotic use stopped in the 24 hours after the intervention vs 16% in the controls. In addition, there is a real but hard-to-quantify economic benefit of reducing the risk of resistance associated with overuse of broad-spectrum antibiotics. Taken together, these benefits are likely to outweigh the very modest cost of the intervention. As a result, we plan to continue and expand such antibiotic counterdetailing efforts in our institution.

Further work will be required to demonstrate the generalizability of an academic detailing approach to other settings and to define the most efficient means to conduct such programs on a larger operational scale. Although development of newer antibiotics may help address antimicrobial resistance in the short term, improving the prescribing of available antibiotics will continue to be a priority throughout the health care system for the foreseeable future.

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